WILLIAM H. STRIETMANN, M. D. (230 Grand Avenue, Oakland).—Doctor Moffitt has referred to a young man with a cystic recurrence of agranulocytosis, associated with a recurrent exacerbation of a stomatitis and especially gingivitis of moderate grade. I have had the opportunity to observe this same patient for the past two years. His "attacks" recur at six-week intervals, but are growing much less severe. The fever does not now exceed 100 degrees, and is often lower. The mouth symptoms are less severe and the leukocyte count may not go below 3000, though the granular elements are always notably reduced, varying in the past two years from 35 to 5 per cent during the height of the exacerbation. This young man was originally the patient of Dr. William S. Thayer and, from recent correspondence with him, I am quite sure that the case will be fully reported in Johns Hopkins bulletin.

Arsenicals must be used with caution because of the tendency to produce a leukopenia.

Of three cases under my observation in the past few years, none have recovered. One of these was treated, according to Doctor Gray's suggestions, with 20 cubic centimeters of leukocytic extract at eight-hour intervals, supplemented by a blood transfusion, but died on the third day.

Again, one should always bear in mind the tendency to recur, remissions of a variable period being not uncommonly noted.

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DOCTOR GRAY (Closing).—Further blood counts on this patient have been checked through the present year. On May 1930: leukocytes, 6900; neutrophils, 62 per cent. On July 1930: leukocytes, 5900; small lymphocytes, 45 per cent; eosinophils, 4 per cent; basophils, 2 per cent; neutrophils, 49 per cent. On September 1930: leukocytes, 3800; small lymphocytes, 15½ per cent; monocytes, 10½ per cent; neutrophils, 47 per cent (200 cells counted). On November 1930: leukocytes, 3050; red blood corpuscles, 4,310,000; hemoglobin, 84 per cent; small lymphocytes, 47 per cent; monocytes, 2 per cent; neutrophils, 51 per cent.

The patient is still feeling perfectly well and has recently had a slight cold, which may have been a factor in depressing the last two leukocyte counts. Because of this gradual drop, I have again started leukocytic extract injections in two cubic centimeter amounts twice weekly, and the patient is now feeling better symptomatically, as regards her strength, energy, etc. The blood count, after four injections, is as follows: On December 5, 1930—leukocytes, 3900; neutrophils, 42 per cent; lymphocytes, 45 per cent; mononuclears, 2 per cent; basophils, 1 per cent.

Regarding Doctor Faulkner's question as to the brand of leukocytic extract used and the method of its preparation, I wish to state that I used the stock preparations of the Vitalait Laboratories, San Francisco, and the E. R. Squibb & Sons, New York.

Since reporting this case at the fifty-ninth annual session at Del Monte, I have been in consultation on three other cases of agranulocytosis; two of which were of such a fulminating character that they expired within twenty-four hours of the time of diagnosis. This was, naturally, before leukocytic extract had any possible chance of being of value. One case in a child less than two years of age was treated with leukocytic extract in adequate dosage with remission of attacks; but eventually the child expired during a relapse when no leukocyytic extract was used. There was some doubt as to this being a true agranulocytosis, but because of the severe primary anemia present, which yielded somewhat, for a period at least, to repeated transfusions, this case was thought to be an aplastic anemia with accompanying leukopenia rather than a true agranulocytosis.

It is hoped that this case report will stimulate others to use the massive dosage of leukocytic extract so that the real efficacy of this treatment may stand or fall under an adequate clinical trial.

ARTHRITIS*

By RODNEY F. ATSATT, M. D.
Santa Barbara

DISCUSSION *by William J. Kerr, M. D., San Francisco; John C. Wilson, M. D., Los Angeles.*

IT may seem presuming for an orthopedic surgeon to address the medical section on the subject of arthritis, but it will be my endeavor to present the matter from the point of view of an orthopedist with the hope that it may be of some value to you.

Each specialist attacks problems in medicine according to his training and train of thought and, in so doing, each one is apt to lose sight of the fact that the symptoms which he treats are but a portion of a general disease picture. The internist may interpret the disease in terms of diet, medication, and disturbances of bowel regulation. The rhinolaryngologist and the dentist think of it as one caused by focal infections. The gynecologist and the urologist may also recognize the disease as one based on focal infection. The orthopedist sees end results with the problems of contractures and malfunctioning joints and further may think in terms of posture, statics and poor body mechanics as factors influencing the course of the disease. The physiotherapist may see the disease as a problem of blood and lymph stasis, bowel stasis, atrophied muscles, adherent tendons, fibrotic capsules, and far too often there is the *bete noir* of *contractures*. Thus we have ofttimes a multiplicity of investigation and therapy without much thought being given to the patient as a whole. It is the thesis of this paper that consideration of the patient as an entity is probably the most important item in the treatment of arthritis.

A DISEASE OF ANTIQUITY

Let us review briefly some of the knowledge of the subject. The disease is of tremendous antiquity, for paleontologists working in Rancho La Brea here in California have brought to light specimens of saber-toothed tigers in which the spines show well-developed hypertrophic arthritis. From this early prehistoric period arthritis may be traced to ancient Egypt, which knew the disability as one of middle and old age, as has been shown by dissection and roentgenograms of mummy specimens. The Greeks and Romans treated arthritis by means of baths and purges. Recent years, however, have seen a determined effort on the part of clinicians and research workers to solve what is probably one of the most widespread and yet one of the most baffling of diseases.

CLASSIFICATION

The most satisfactory classification is the old one which recently has been adopted by the American Committee for the Control of Rheuma-

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tism, dividing the disease into the atrophic and hypertrophic groups. This is similar to the pathological classification of Nichols and Richardson, who called the divisions proliferative and degenerative.

Atrophic or Proliferative Group.—In the atrophic and proliferative form, as you know, there develops from the synovial membrane a pannus-like growth which spreads out over the cartilage and eventually destroys it. Fibrous changes take place in the synovial membrane and capsule, often giving a marked spindle-shaped periarticular thickening. This form of the disease is progressively polyarticular and often advances to complete ankylosis. It usually attacks the young or middle-aged individual and is extremely chronic.

Hypertrophic or Degenerative Group.—In the hypertrophic or degenerative form, the cartilage softens and is eroded to give a joint in which the articulation is between bare eburnated bones. The joint itself is irregularly enlarged due to the formation of osteophytes around the joints as illustrated by Heberdeen's nodes on the fingers. The hypertrophic form appears in the later decades of life usually after the age of forty-five. It is subject to periods of exacerbation and remission, the pain depending largely upon the state of the inflammatory reaction in the soft tissues of the joint and those surrounding the osteophytic spurs.

ETIOLOGY

The etiological factors involved may be many. Whether this is a disease of focal infection, metabolic disturbance including dysfunctions of the endocrine system, allergic phenomena, absorption from the gastro-intestinal tract or the result of traumatism is an open question.

From the standpoint of focal infection there always must be considered the well-known triad of teeth, tonsils, and sinuses, together with infections of the bowels, urinary tract, and pelvis. Furthermore, focal infections may effect the joint changes by one of three ways—direct passage of organisms to lodgment in the joints; affinitive absorption by the joints of circulating bacterial toxins from distant foci; and lastly the possibility of joint damage through the deleterious effect of bacterial toxins on the general body metabolism.

From the metabolic standpoint there must be considered the effect of the ingestion of increased amounts of carbohydrate and nitrogenous foods and their digestion. Dysfunctions of the endocrine system, especially the thyroid gland, are another problem in metabolism.

In considering toxic absorption from the gastro-intestinal tract as a cause of arthritis there must be borne in mind not only the possibility of bacterial intoxication, but the possibility of partially split proteins reaching the large bowel. Here there is no protective erepsin ferment mechanism, and these partially split proteins may pass into the blood stream while in the toxic form.

Traumatism plays a part in nearly every case of hypertrophic arthritis in that while the disease may have been quietly advancing for some years (perhaps even due to small repeated strain traumata) suddenly there comes some distinct major or minor injury which so aggravates the local condition that it is brought to the attention of the patient for the first time.

In the estimation of some, there is an underlying background which many times dominates the picture and actually controls the course of the disease, making it one of progression or regression, as the case may be. For want of a better term, this background will be called resistance. It is perhaps impossible to define, but among other things, of course, ideal resistance would include a condition of well-being wherein there was no absorption or metastasis from focal infection, no indigestion with unbalanced metabolism or toxic assimilation and no debilitation from intercurrent disease or from exposure to wet or cold.

Closely coupled with these physical and chemical conditions influencing resistance and really an important part of it is the physiological factor of fatigue. Fatigue is a relative state and is induced in various patients by a variety of causes and in varying intensity by similar events. There is a nicety of balance between resistance and fatigue and when the boundary line between fatigue and overfatigue is crossed, the immediate reaction is a lowering of active vitality. This lowered vital state may be promptly reflected in the condition of the arthritic patient, especially in the atrophic type. More and more is fatigue becoming recognized as an etiological factor in arthritis, and it is being learned gradually that the avoidance of this reaction is oftentimes of more importance than some seemingly necessary procedure of treatment.

Allied with the effect of fatigue as an etiological factor in atrophic arthritis, is the rôle of hard work or hard play in the production of the hypertrophic type, for often this form is seen in those individuals who have been strenuous in their endeavors. Some observers maintain that, in the early stages at least, this hypertrophic form does not represent so much an arthritis or joint inflammation as it does an effort on the part of nature to strengthen the ligamentous and capsular attachments around the joint periphery by ossification. Thus intense activity may be prolonged past the period of middle life with apparent immunity until some wrench or fall may bring to light a process which is far advanced.

TREATMENT

The problem of treatment in arthritis is a complex affair. Naturally with the wide variety of etiological agents which have been considered, the forms of treatment must be many, and by their very multiplicity they announce that they are in the main unsatisfactory. Then, too, sequelae may persist long after the distinct etiological factor has been removed and thus contribute to the chronicity of the disease.

Tonsillectomy would be advised in every case of arthritis in which pus can be demonstrated in the tonsillar crypts. An optimum time may be chosen, however, so that the operation may not be an added straw to an already breaking resistance. Even when the tonsils appear innocuous their removal is sometimes advisable, especially in cases of cervical or temporomandibular arthritis.

Dental examination and roentgenology is perhaps the next important step. Wholesale extraction of teeth is usually ill advised, but when the combined opinions of the dentist, the roentgenologist, and the physician agree that certain teeth are suspicious, then extraction is in order. Root infections always call for extraction and not treatment, while in pyorrheal infections, teeth may usually be saved by proper and efficient treatment.

With infection of the accessory nasal sinuses as the cause of arthritis, there exists a serious situation, for complete eradication of such a focus is most difficult. In spite of the chronicity of such focal infections and the accompanying arthritis, persistent efforts should be made in treatment, either radical or conservative.

Focal infection of the kidney, bladder, and tubes are seldom important contributory factors, but treatment of infections of the cervix, prostate and seminal vesicles often leads to remarkable improvement.

The gastro-intestinal tract must be considered from two viewpoints—that of focal infection and of toxic absorption. Focal infection, with the possibilities of passage of either bacterial toxin or the organisms themselves, may be present with inflammation of the gall bladder, the appendix, one or more diverticulae, or of the bowel wall itself. In the first two conditions, surgery is probably always indicated; with diverticulitis it is often indicated; but where the infection is in or on the bowel wall, medication, change of flora, bowel lavage or diathermy may be the treatments of choice.

Toxic intestinal absorption again may be considered from two angles—the absorbable toxin may be produced by bacterial decomposition of slow-moving ingested material or it may be produced by incompleted normal digestive processes. In the former instance, change of flora may be made by implants of innocuous saprophytic organisms or by variation of the foods ingested, bowel lavage, increasing the movement of the fecal stream through administration of sodium phosphate, psylla seeds, mineral oil, agar or some such device, abdominal massage or the use of sinusoidal current stimulation.

When the toxin is produced by incomplete digestion, the administration of pancreatin or pancreatin and diastase in enteric coated granules will often so advance the small bowel digestion that complete splitting of the proteins will take place in the proper situation, that is, in the small bowel, and the partially split products will not reach the large bowel where there is no erepsin protective mechanism.

Medication in the arthritides is of relatively less importance than are some of the other methods of treatment. The most useful drug is probably some form of salicylic acid. There seems to be almost a specificity of this drug for acute arthritis and this benefit is quite aside from its analgesic action. Thyroid dysfunctions, as evidenced by a lowered basal rate, accompany many cases of arthritis and thyroid extract may be given to these cases in well-regulated amounts, often with distinct improvement. It is not clear whether this product acts by speeding up the general metabolic processes and thus overcoming a lowered oxidation level or whether the improvement in the joints is due to increased local circulation.

Arsenic in the form of cacodylate is often beneficial, but here the improvement is due to the building of general health rather than to any specific effect on the arthritis. Numberless so-called specific drugs are on the market, but in none have the claims of the manufacturers been properly substantiated.

Diet limitations have undergone many changes in recent years. The strict abstinence from meat is no longer considered wise. There is considerable scientific background for the belief that a low carbohydrate intake is beneficial. Certain it is, however, that the diet must be broad enough in character and ample enough in amount to be one of the factors in increasing bodily resistance, for without general well-being, the fight against arthritis is a losing one. Food allergy plays a part in the arthritic regimen, for in some cases certain foods must be avoided. It has been found, however, that the use of pancreatin often makes it possible for the patient to eat safely many of the disturbing foods.

Nonspecific protein injections, such as typhoid vaccine or milk, have some place perhaps in acute and subacute arthritis, but they are usually of little permanent avail in chronic cases. Vaccine therapy similarly has not fulfilled the expectations of the enthusiasts, even when autogenous vaccine is employed, though the latter occasionally gives striking results. It is probably true that much of the value of vaccine therapy lies in its nonspecific protein shock with its increase in local circulation and temperature. Another biological form of treatment is found in the use of so-called specific antisera and these are sometimes of value.

Physiotherapeutic measures are of great importance for the relief of pain and also for actual improvement of the disease. Baking and infrared radiation are forms of dry heat which stimulate the circulation of both blood and lymph and perhaps raise the oxidation level of the local metabolic processes. Diathermy is another effective form of heat administration. The whirlpool

bath, the contrast bath, and the Epsom salt soak are also especially designed to be stimulating to local circulation.

Massage is of great benefit when properly applied and of great harm when used improperly. When given correctly it stimulates the circulation of blood and tissue fluids, and partially takes the place of the muscular exercise which is prohibited by the acute joints. The massage should always be above and below the joints, with the minimum of effleurage over the joint itself. Atrophy of muscles should be treated by massage and active exercises, and limitation of motion by active and carefully guarded passive exercises and stretching.

Quartz lamp, carbon lamp, and heliotherapy are also of distinct value by building up resistance. It must be borne in mind, however, that none of these measures should greatly fatigue the patient, for general health must not be allowed to suffer for even the most important measures of therapy.

The orthopedist with his knowledge of body mechanics is often called into service with the arthritic patient. It is usually to the best interests of the patient to do this early, for an ounce of prevention is worth a pound of cure in the matter of contractures and deformities. Pronated feet, inefficient, unstable or contracted joints, stiffened or crooked spines, atrophied muscles, secondary neuritides—all these conditions need the scrutiny of the competent orthopedic surgeon. The postural aspect of body mechanics deserves the closest attention from trained individuals whether the patient is erect or supine. The orthopedist should see further that inefficient, irritated joints are not used beyond the limits of safe physiological action, for nothing is more destructive to a joint than pushing its use beyond the limits of pain.

In closing, it is to be remembered that general good health and resistance with well-balanced diet and well-balanced therapy are perhaps the most important factors in the treatment of arthritis. Every case is a problem of its own and each regimen must be chosen with the greatest of care and specificity, for there is no routine cure-all for this disease.

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DISCUSSION

WILLIAM J. KERR, M. D. (University of California Hospital, San Francisco).—It is very refreshing to hear a paper such as this one by Doctor Atsatt. In the past too much attention has been given to supposed specific methods of treatment of arthritis, and far too little attention to the care of the patient.

Foci of infecion may not be a chief cause of arthritis. Anyone who has had many patients under observation with arthritis will, I think, be struck by the frequency with which so-called "foci of infection" develop some time after the patient has shown symptoms of arthritis. This would suggest that perhaps the general disturbance which brought about the arthritis also reduced the resistance of the patient to infection which allowed these conditions to arise at a subsequent time. While the presence of foci of infection may further endanger the individual, yet I think it would be unwise to direct our attention to the foci and neglect to improve the general health of the individual.

Practically all of the methods of treatment—*e. g.*, tonsillectomies, extraction of teeth, vaccine therapy, and other forms of "shock therapy"—act very much alike. Something takes place following these procedures which probably leads to vasodilatation through paralysis of the vasoconstrictures, leading to improved peripheral circulation over a considerable period of time. Some authorities go so far now as to suggest that sympathectomies are useful in these cases since they bring about paralysis of the vasoconstrictors and improved circulation to the joints. We cannot be certain that this method of treatment will have more than temporary effect, nor can we be certain what the end results in such cases will be.

I think that Doctor Atsatt. has covered well the various methods of attack in arthritis. I have used practically all those which he has enumerated, and have found that if at the same time I pay a good deal of attention to the general health, avoiding fatigue, using a well-balanced diet, taking due care of joints and the prevention of deformities, that the patient will improve remarkably. One always has the hope in the treatment of this disease that if he keeps on doing something rational and which is not in itself harmful and is conscientious about it, bye and bye the patient will improve.

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JOHN C. WILSON, M. D. (1136 West Sixth Street, Los Angeles).—Doctor Atsatt's paper covers a difficult field with extraordinary thoroughness and with commendable conservatism. In the literature on this subject we encounter a varied and confusing array of contradictory opinion, much of which emanates from enthusiastic proponents of some particular method of treatment. In no other condition is there greater need of studying the patient as a whole and of treating the patient instead of the disease. The general health must be improved to the utmost possible degree, full information must be obtained concerning the state of the body metabolism, and obscure etiologic factors must be searched for carefully in order that our therapeutic efforts may be appropriate for the individual case. Our most important and difficult duty in the more severe cases lies in supporting the patient's morale through the prolonged and discouraging ordeal which he has to suffer.

Too little attention is paid to the very important matter of preventing deformities and contractures. If this be kept in mind from the earliest stages of the disease, a great deal of needless disability can be avoided.

Surgery involving arthritic joints requires a nicety of clinical judgment. Surgical intervention following an injury in the presence of chronic arthritis, which is often latent and unrecognized, especially if compensation is involved, is likely to result in a prolonged and intractable disability. After an acute arthritis has become quiescent, however, a great deal of benefit can be derived from operations designed to remedy contractures or deformities and in suitable cases an arthrolysis or synovectomy will result in a remarkable improvement in function. On the other hand, a surgical fusion of a damaged joint frequently offers the best functional result and should be resorted to when extensive erosion of the articular surfaces has taken place.

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DOCTOR ATSATT (Closing).—I wish to thank Doctors Kerr and Wilson for their discussions.

In closing, I wish to reiterate part of my thesis—that body resistance is of fundamental importance in the treatment of arthritis and overfatigue goes far in breaking down and keeping down the optimum conditions for the arthritic patient.